sion on ECG and a planar thallium (TL) perfusion defect during maximal treadmill testing was a potent independent predictor of future coronary events (CE) over a mean follow-up of 4.7 years in 407 asymptomatic volunteers aged 40–96 years (mean = 60) from the Baltimore Longitudinal Study of Aging (Circulation 1990;81:428). To determine the longer term prognostic significance of SI in this population, we examined the incidence and predictors of CE over a mean follow-up of 9.2 years. A total of 61 CE developed (32 cases of new angina pectoris, 17 non-fatal myocardial infarctions, 12 cardiac deaths). Events occurred in 15% of subjects with both negative ECG and TL responses, 30% of those with either a positive ECG or TL result, and 48% of those in whom both tests were positive ($p < 0.001$). By proportional hazards analysis, older age (relative risk [RR] = 2.3 per 15 year increment), male gender (RR = 2.2), hypertension (RR = 2.5), shorter exercise duration (RR = 0.91 per minute), and a concordant positive ECG and TL response (RR = 2.5) were significant independent predictors of CE. Hard CE, i.e. myocardial infarction or cardiac death, were predicted by older age (RR = 3.1), male gender (RR = 2.8), current smoking (RR = 3.0), plasma cholesterol (RR = 1.01 per mg/dl), fasting plasma glucose (RR = 1.01 per mg/dl) and a concordant positive ECG and TL (RR = 3.4). Thus, at a mean follow-up of over 9 years, exercise-induced SI remains a potent predictor of future CE in apparently healthy volunteers, independent of conventional risk factors.

2:15

716-2 Myocardial Ischemia Induced by Mental Stress Predicts a Poorer Prognosis in Patients with Coronary Artery Disease

Wei Jiang, James A. Blumenthal, Steven E. McNulty, Michael W. Hanson, R. Edward Coleman, David J. Frid, Robert A. Waugh, James J. Morris, Christopher M. O'Connor. *Duke University Medical Center, Durham, NC*

Although it is clear that mental distress elicits myocardial ischemia, the relationship of mental stress-induced myocardial ischemia (MSI) to prognosis in patients with CAD is unknown. 130 CAD patients with stable angina underwent a series of mental stress and exercise tests using radionuclide ventriculography and standard 12-lead ECG, then were followed for one year. Myocardial ischemia was defined as a new wall-motion abnormality, ejection fraction (EF) decrease >5%, or ST-segment depression ≥0.1 mV from baseline. Cardiac events (CE) were defined as CABG, PTCA, unstable angina admission requiring angiography (UA), nonfatal myocardial infarction (NMI), and cardiac death.

Of the 130 patients, 50% had both MSI and exercise-induced ischemia (ESI), 18% experienced MSI alone, and 18% had ESI alone. Of the 117 patients achieving one-year follow-up, 20 suffered various CE: 19 had UA, 9 had PTCA, 4 had CABG, 2 had NMI, and 1 died. Logistic regression analyses were performed to examine the possible relationships among age, baseline systolic blood pressure (SBP), baseline EF, MSI, ESI and CE. Results showed that baseline SBP and MSI, but not ESI, were univariable predictors of CE (see Table). Multivariable logistic models were then used, with age, baseline SBP, and baseline EF as covariables, to determine if the addition of either MSI or ESI provided prognostic information in predicting CE. MSI was independently predictive of CE after adjustment for the covariables.

Univariable	X^2	p Value
Age	0.49	0.48
Baseline SBP	5.32	0.02
Baseline EF	0.001	0.97
MSI	4.77	0.03
ESI	0.48	0.49

In *conclusion*, MSI may have greater prognostic potential than ESI for a specific population of CAD patients.

2:30

716-3 Prognostic Significance of Transient Ischemic Episodes; Response to Treatment Shows Improved Prognosis. Results of the TIBBS-follow-up

Th. v. Arnim, TIBBS (Total Ischemic Burden Bisoprolol Study) investigators. *Red Cross Hospital, Munich, Germany*

TIBBS is a multi-center trial in which patients with stable angina pectoris and a positive exercise ECG were selected for randomized medical treatment when they showed transient ischemic episodes (TIE) on 48-h-ambulatory ECG monitoring (AECG). The follow-up study at 1 year investigates the implications for the prognosis of the patients.

Of 621 patients screened on the basis of history of stable angina pectoris and positive exercise ECG, 565 had technically sufficient 48-h-AECG, and 193 showed 0 or 1 TIE (1 mm, 1 min, 1 min. apart) 152 showed 2–6 TIE, 153 showed >6 TIE. Follow-up at one year was >90% complete. Physicians in charge of the patients were unaware of the results of AECG.

Patients with 0–1 TIE had less cardiac events (death, AMI, CABG, PTCA, hospitalisation for unstable A.p.) at one year (11.9%) compared to patients with 2–6 TIE (+26.3%) or patients with >6 TIE (30.5%) ($p < 0.001$).

Of 268 randomized patients, those 90 patients who had shown response to medical treatment with 100% reduction of TIE during the 8-week active phase of TIBBS (treatment with Bisoprolol 10 mg/20 mg o.d. vs. Nifedipin slow release 2 × 20/2 × 40 mg b.i.d.) had better prognosis: 17.8% events compared to 30.6% events in patients with less or no reduction of TIE ($p < 0.025$). Patients who responded with 50% reduction of TIE showed only a trend towards reduced risk of events: 23.3% vs 30.9% ($p < 0.117$).

Conclusion: AECG in patients with stable angina pectoris and positive exercise ECG selects patients with increased risk of cardiac events. Patients who do not respond to medical treatment with reduction of TIE are at further increased risk.

2:45

716-4 Placebo Treatment Reduces Both the Number of Ischemic Episodes and Duration of Ambulatory Silent Myocardial Ischemia in Patients with Stable Angina Pectoris

Udho Thadani. *University of Oklahoma HSC, Oklahoma City, OK*

Ambulatory silent myocardial ischemia occurs frequently in patients with stable exertional angina pectoris. It is widely accepted that a medication has antiischemic effects if it reduces either the number or the duration of silent myocardial ischemic episodes in comparison to pretreatment values. Effect of monotherapy with placebo on silent myocardial ischemia in 33 patients who took part in a parallel group investigational drug study and were assigned to the placebo arm of the study form the basis of this investigation. After discontinuation of all antianginal medications patients received two weeks of single blind placebo treatment followed by four weeks of double blind placebo treatment. Ambulatory holter monitoring was performed for 48 hours after two weeks of single blind placebo treatment and again after 4 weeks of double blind placebo treatment. The median value of silent myocardial ischemia attack rate during single blind placebo treatment was 7.2 episodes per 48 hours and decreased during double blind placebo treatment to a median rate of 3.1 episodes per 48 hours ($P < 0.004$; 95% CI, −5.41, −1.0). Similarly the duration of silent myocardial ischemic episodes decreased by a median of 16.1 minutes per 48 hours ($P < 0.001$; 95% CI, −35.7, −6.2 minutes) during double blind placebo treatment from a median value of 24.8 minutes per 48 hours during single blind placebo treatment. *Conclusion:* placebo monotherapy had a marked influence on ambulatory silent myocardial ischemia and reduced both the duration and number of silent myocardial ischemic episodes in patients with stable angina pectoris. These findings have important implications for interpretation of studies in which the effects of active treatment on silent myocardial ischemia are compared to baseline pretreatment values.

3:00

716-5 Treatment of Silent Ischemia in Unstable Angina: A Randomized Comparison of Sustained-release Verapamil Versus Metoprolol

Narendra Singh, Dmitry Mironov, Shaun Goodman, Chris D. Morgan, Anatoly Langer. *St. Michael's Hospital, Toronto, Ontario, Canada*

Silent ischemia is a frequent finding in pts with unstable angina (UA) which portends a poor prognosis. We compared the efficacy of sustained-release verapamil and metoprolol (M) in the treatment of silent ischemia and studied whether detection of silent ischemia was related to unfavourable outcomes irrespective of treatments. Consecutive pts with UA were randomized to therapy with verapamil or metoprolol and all received nitrates, heparin and aspirin by protocol. ST shift (≥1 mm, 60–80 msec after J point and separated by ≥1 min from other episodes) was detected on 72 hr Holter monitoring (leads AVF, V_2, V_5).

There were 37 pts in the verapamil (218 ± 89 mg/day) and 40 pts in the metoprolol (88 ± 24 mg/day) group. The two groups were similar in baseline characteristics. Recurrent angina episodes were more frequent in the verapamil group (29 vs 12, $p = 0.05$). Overall 26 (34%) pts had 100 episodes of ST shift, 75% ST↓, 95% silent. Comparing the verapamil vs metoprolol group, there was no difference in the frequency (51 vs 49 episodes, $p = 0.9$) and duration (23 ± 48 min vs 18 ± 50 min, $p = 0.6$) of ST shift episodes. 20 in-hospital unfavourable outcomes (5-MI, 15-urgent revascularization) were distributed equally between verapamil and metoprolol pts. However, pts with unfavourable outcomes irrespective of treatment more often had ST shift (50% vs 28%, $p = 0.07$), and with longer duration (40 ± 69 vs 13 ± 38 min, $p = 0.03$). Pts with ST shift ≥60 min had a 60% probability of unfavourable outcome compared with 33% for ST shift between 1–59 min and 20% for pts without ST shift ($p = 0.04$).

Conclusions: Metoprolol appears to reduce symptomatic ischemia better than verapamil, but no difference in silent ischemia and unfavourable outcomes was seen. SI is common (34%) in UA despite heparin and aspirin therapy. Detection of SI is related to prognosis irrespective of treatment and may be useful for early non-invasive risk stratification.

3:15

716-6 Nocturnal Blood Pressure and Myocardial Ischemia in Patients with CAD

Joachim Müller, Ulrich Tönnesmann, Stefan Schaupp, Ingomar-Werner Franz. *Klinik Wehrawald, Todtmoos, Germany*

Objective: It is well known that B.P. rises during the day and decreases during the night. However, patients with CAD have an impaired coronary flow reserve and they may be endangered by myocardial ischemia due to a substantial reduction in nocturnal diastolic B.P. The purpose of the study was to test this hypothesis. *Methods:* In 103 patients (82 ♂, 21 ♀, mean age 60 ± 8 years) with documented CAD a 24-h ambulatory blood pressure monitoring (SpaceLabs 90 202) and a 24-h Holter monitoring with ST-segment analysis (Pathfinder V) was simultaneously performed. The patients were arbitrarily divided into three groups with regard to their mean nocturnal diastolic B.P. (10.00 p.m. – 6.00 a.m.): Group 1: <60 mmHg (58 ± 3) group 2: 61 – 70 mmHg (66 ± 3), group 3: 71 mmHg (78 ± 7). There were no significant differences between the three groups concerning age, sex distribution, coronary status and therapy. *Results:* In group 1 86.2% of the patients had nocturnal episodes of ST-segment depression compared with 50% of group 2 and 33.3% of group 3. Group 1 patients revealed a significant higher incidence of episodes (2.7 ± 2.4/night) compared with 1.2 ± 1.8 ($p < 0.01$) and 0.6 ± 1 ($p < 0.001$) of group 2 and 3, respectively and a significant ($p < 0.001$) longer duration (1608 s versus 392 s and 143 s, respectively). Group 1 patients had a significantly greater reduction in nocturnal diastolic B.P. with 14.3 ± 6 mmHg compared with 11.5 ± 6 mmHg ($p < 0.05$) and 6.6 ± 5 mmHg ($p < 0.001$), respectively.

Conclusions: In patients with CAD a low nocturnal diastolic B.P. profile (<70 mmHg) goes along with a higher incidence and longer duration of silent ischemic episodes. A drop in perfusions pressure seems to be responsible for that and should be taken into account when treating such patients with antihypertensive or antiischemic drugs.

717 Percutaneous Balloon Mitral Valvotomy

Monday, March 20, 1995, 2:00 p.m.–3:30 p.m.
Ernest N. Morial Convention Center, Room 6

2:00

717-1 Elevated Left Ventricular End-Diastolic Pressure in Mitral Stenosis: Reduction After Valvuloplasty

Roderick J. Sawyer, John D. Carroll, Ted Feldman, Thomas N. Levin, Gerald Dorros, North American Inoue Investigators. *The University of Chicago Hospital, Chicago, IL*

Traditionally, an elevated LVEDP in mitral stenosis has implied coexistent aortic valve disease, coronary artery disease, or myocardial disease and has been a predictor of poor outcome after mitral valvuloplasty (BMV). We first examined our local population of BMV (n = 77) and found that aortic and coronary disease did not account for the elevated LVEDP in the majority of patients. Secondly, we examined the Inoue BMV database. Group I (n = 844) had pre-BMV LVEDP ≤ 15 mmHg while group II (n = 200) had an LVEDP > 15 mmHg. After BMV a rise in LVEDP occurred in group I (pre: 9.9 ± 3.3 mmHg vs post: 12.5 ± 8.6 mmHg, $p < 0.05$) as well as a decrease in mean LAP from 23 mmHg to 17 mmHg, $p < 0.05$). In contrast, group II had a fall in LVEDP (pre: 22.7 ± 15.2 mmHg vs post: 19.8 ± 11.4 mmHg, $p < 0.05$) as well as a decrease in LAP (28 mmHg to 24 mmHg, $p < 0.01$).

A subgroup studied at six months post-BMV revealed no change in group I (n = 105) LVEDP (post: 11.5 ± 5.4 mmHg vs 11.8 ± 4.7 mmHg, p = NS) while group II (n = 22) had a progressive fall (post: 19.9 ± 4.8 mmHg vs 13.8 ± 3.8 mmHg, $p < 0.01$). There was no correlation between NYHA class at six months and the pre or post BMV LVEDP.

Conclusion: An increased baseline LVEDP in mitral stenosis is not a predictor of poor outcome after mitral valvuloplasty. The fall of LVEDP supports the claim that BMV improves LV chamber compliance perhaps by untethering the restricted LV.

2:15

717-2 Echocardiography Can Predict Patients Who Develop Severe Mitral Regurgitation Following Percutaneous Mitral Balloon Valvuloplasty

Luis R. Padial, Nelmacy Freitas, Alex Sagie, Arthur Weyman, Mary Etta King, Robert A. Levine, Igor F. Palacios. *Massachusetts General Hospital, Boston, MA*

Although specific echocardiographic features of the mitral valve (MV) have been shown to predict the likelihood of a successful outcome of percutaneous mitral valvuloplasty (PMV), they do not identify those patients who are more likely to be a risk for significant mitral regurgitation (MR) post- PMV.

Based on pathologic data from patients who developed severe post-PMV-MR, an echocardiographic score was developed. (MR-Echo Score) which included uneven distribution of thickness and calcification of both mitral leaflets, degree of commissural disease and subvalvular involvement. Each component was graded fro 0–4 and a total score (0–16) was calculated. Intraobserver and interobserver variability for score assessment were 6% and 7% respectively.

From 566 consecutive patients who underwent PMV, 36 (6.5%) developed severe post-PMV MR (>3+ by angiography.) The MR-Echo Score was applied to 31 of these patients (28 women; mean age 54 + 14 yr.) for whom pre-PMV echocardiograms were available and 31 randomly selected patients who did not develop severe post-PMV MR but were matched for age, sex, pre-PMV MV area and degree of MR. The total MR- Echo Score was significantly greater in the severe MR group (11.7 ± 1.9 vs. 8 ± 1.2; $p < 0.001$). Using a total score ≥10 as a cutoff point for predicting severe post PMV MR, a sensitivity of 90 ± 5% and a specificity of 97 ± 3% were obtained. Stepwise logistic regression analysis identified the MR-Echo Score as the only independent predictor for the development of severe post-PMV MR ($p < 0.0001$).

Conclusions: Specific morphologic features of the mitral valve apparatus in mitral stenosis as identified in this new MR-Echo Score predict the development of severe post PMV MR and therefore can be useful in the selection of patients for PMV.

2:30

717-3 Do All Patients Undergoing Inoue Balloon Mitral Valvotomy Need Transesophageal Echo (TEE) to Exclude Left Atrial Thrombus?

Jai J. Patel, Robin B. Dyer, Ravi G. Pillay, Miroslav J. Munclinger, Abdul S. Mitha. *Cardiac Unit, Wentworth Hospital/University of Natal, Durban, South Africa*

To assess merits of TEE and transthoracic echo (TTE) to exclude left atrial body (B) or appendage (A) thrombus (T) before valvotomy, we performed both in 151 consecutive patients (mean age 30) with tight mitral stenosis and NYHA II/III disability (Group I).

	T detected on TEE	T suspected on TEE	Confirmed Surgery	No T at Surgery	PMV
(i)	5 (B+ –A)	5	3	–	1
(ii)	5 (A)	3	5	–	–
(iii)	3 (A)	–	–	3	–
(iv)	3 (A)	2	–	–	2

In (i), 1 pt refused surgery and 1 had PMV after 3 mths of warfarin. In (iv), 2 pts had PMV and 1 no procedure. Thus 10.5% pts showed thrombus on TEE; of these 81% were in AF and 3 were in SR. Following on this experience, the next 165 similar consecutive pts had TEE before PMV only if T was suspected on TTE. Group II:

	T suspected on TTE	T detected on TTE	Confirmed at Surgery
(i)	7 (B+ –A)	7	7
(ii)	20 (A)	11	–

All 11 pts in (ii) with TEE thrombus had uneventful PMV. Thus only 16% had TEE. Of 38 pts having PMV without TEE, minor embolic episodes occurred in 3. All 3 had no evidence of T on post event TEE.

Conclusion: In young pts carefully performed TTE is a useful screening procedure before PMV. TEE is not mandatory and should be performed if T suspected on TTE to exclude left atrial body thrombus as Inoue PMV is safe in presence of appendage thrombus.